

ORIGINAL ARTICLE

Hospital variation in Textbook Outcomes following curative-intent resection of hepatocellular carcinoma: an international multi-institutional analysis

Diamantis I. Tsilimigras^{1,*}, Rittal Mehta^{1,*}, Katiusha Merath^{1,*}, Fabio Bagante^{1,2}, Anghela Z. Paredes¹, Ayesha Farooq¹, Francesca Ratti³, Hugo P. Marques⁴, Silvia Silva⁴, Olivier Soubrane⁵, Vincent Lam⁶, George A. Poultsides⁷, Irinel Popescu⁸, Razvan Grigorie⁸, Sorin Alexandrescu⁸, Guillaume Martel⁹, Akiile Workneh⁹, Alfredo Guglielmi², Tom Hugh¹⁰, Luca Aldrighetti³, Itaru Endo¹¹ & Timothy M. Pawlik¹

¹Department of Surgery, The Ohio State University Wexner Medical Center, Columbus, OH, USA, ²Department of Surgery, University of Verona, Verona, ³Department of Surgery, Ospedale San Raffaele, Milano, Italy, ⁴Department of Surgery, Curry Cabral Hospital, Lisbon, Portugal, ⁵Department of Hepatobiliopancreatic Surgery, APHP, Beaujon Hospital, Clichy, France, ⁶Department of Surgery, Westmead Hospital, Sydney, Australia, ⁷Department of Surgery, Stanford University, Stanford, CA, USA, ⁸Department of Surgery, Fundeni Clinical Institute, Bucharest, Romania, ⁹Department of Surgery, University of Ottawa, Ottawa, Canada, ¹⁰Department of Surgery, The University of Sydney, School of Medicine, Sydney, Australia, and ¹¹Yokohama City University School of Medicine, Yokohama, Japan

Abstract

Background: Composite measures such as “Textbook Outcome” (TO) may be superior to individual quality metrics to assess surgical care and hospital performance. However, the incidence and factors associated with TO after resection of HCC remain poorly defined.

Methods: Hospital variation in the rates of TO, factors associated with achieving a TO and the impact of TO on long-term survival following resection for HCC were examined using an international multi-institutional database.

Results: Among 605 patients who underwent curative-intent resection of HCC, the unadjusted incidence of TO ranged from 50.9% to 77.7%. While achievement of each individual quality metric was relatively high (range, 74.5–98.0%), an overall TO was achieved among only 62.3% (n = 377) of patients. At the hospital level, TO ranged from 54.3% to 72.9%. Patients with BCLC-0 HCC (referent BCLC-B/C; OR: 4.17, 95%CI: 1.62–10.7) and ALBI grade 1 (referent ALBI grade 2/3; OR: 1.49, 95%CI: 1.06–2.11) had higher odds of achieving a TO. On multivariable analysis, TO was associated with improved overall survival (HR: 0.60, 95% CI: 0.42–0.85).

Conclusion: Roughly 6 in 10 patients achieved a TO following resection for HCC. When achieved, TO was associated with better long-term outcomes. TO is a simple composite measure of both short- and long-term outcomes among patients undergoing resection for HCC.

Received 5 July 2019; accepted 2 December 2019

Correspondence

Timothy M. Pawlik, Department of Surgery The Urban Meyer III and Shelley Meyer Chair for Cancer Research Professor of Surgery, Oncology, Health Services Management and Policy The Ohio State University, Wexner Medical Center, 395 W. 12th Ave., Suite 670, USA. E-mail: tim.pawlik@osumc.edu

Introduction

Traditional assessment of quality for complex surgery has relied mainly on analysis of individual healthcare outcome parameters such as serious complications, length of hospital stay,

readmission and mortality.¹ With the increasing need for more reliable quality indicators related to surgical care, the use of composite quality measures have been proposed as potentially superior to individual measures to assess hospital performance.^{2–5} Among the different approaches available for developing composite measures, the “all-or-none” approach to various outcome parameters has been described as the most

* These authors contributed equally to this work.

consistent with a patient-centered perspective.⁶ Specifically, such a composite measure -the so-called “Textbook Outcome” (TO)-represents the “textbook” hospital course following surgery and has been proposed as a metric that aligns the most with patient expectations around an “optimal” experience.⁷ TO incorporates important individual outcome parameters related to the surgical episode, providing a comprehensive summary of overall quality of care that allows for a holistic assessment of variation among patient- and hospital-based outcomes.

Hospital variations in TO have been demonstrated among patients undergoing surgery for colorectal cancer, as well as vascular disease.^{7–11} Recently, our own group reported on variation in TO rates among patients undergoing resection of intrahepatic cholangiocarcinoma (ICC), as well as among Medicare patients undergoing hepatopancreatic surgery.^{7,11} To the best of our knowledge, no study has investigated the variation in rates of TO specifically among patients undergoing surgical resection of hepatocellular carcinoma (HCC). Assessing TO among patients with HCC may be particularly important as this group of patients often has multiple comorbidities (e.g. cirrhosis, portal hypertension, etc.) and a higher than average incidence of perioperative complications.¹² Therefore, the objective of the current study was to define the incidence of TO among patients undergoing curative-intent resection of HCC at tertiary hepatobiliary centers using an international multi-institutional database. In addition, factors associated with the receipt of a TO following surgery for HCC, as well as the association of TO with long-term survival were assessed.

Methods

Data sources and study population

Patients were identified using a multi-institutional database that included 11 major tertiary hepatobiliary institutions: The Ohio State University Wexner Medical Center, Columbus, OH, USA; Yokohama City University School of Medicine, Yokohama, Japan; University of Verona, Verona, Italy; Ospedale San Raffaele, Milano, Italy; Curry Cabral Hospital, Lisbon, Portugal; APHP, Beaujon Hospital, Clichy, France; Westmead Hospital, Sydney, Australia; Stanford University, Stanford, CA, USA; Fundeni Clinical Institute, Bucharest, Romania; University of Ottawa, Ottawa, Canada; The University of Sydney, School of Medicine, Sydney, Australia. Patients who underwent curative-intent resection of HCC between 2000 and 2015, who had information on type of surgical procedure, surgical margins, postoperative complications, reoperation, length-of-stay (LOS), hospital readmission, and 90-day mortality were included. The study was approved by the Institutional Review Board of each participating institution.

Data collection

Demographic and clinical data included sex, age, American Society of Anesthesiologists (ASA) class, Charlson Comorbidity

score, Barcelona Clinic Liver Cancer (BCLC) stage, history of cirrhosis, type of resection (i.e. minimally invasive or open), history of hepatitis B (HBV) or C (HCV) virus infection, tumor grade, extent of resection (i.e. minor or major), laboratory values (i.e. platelet count, albumin, alpha-fetoprotein (AFP)), neutrophil-to-lymphocyte (NLR) ratio, number of tumors, pathologic data (i.e. lympho-vascular invasion, liver capsule involvement), albumin-bilirubin (ALBI) grade, and length-of-stay. Patients were categorized into BCLC stages¹³ according to the latest European Association for the Study of Liver guidelines.¹⁴ Major hepatectomy was defined as resection of 3 or more Couinaud segments.¹⁵ ALBI score was calculated using the formula: $[\log_{10} \text{bilirubin } (\mu\text{mol/L}) \times 0.66] + [\text{albumin } (\text{g/L}) \times -0.085]$; patients were categorized as ALBI grade 1 ≤ -2.60 , grade 2 ≥ -2.60 and ≤ -1.39 , and grade 3 ≥ -1.39 , as previously reported.¹⁶

Textbook outcome

TO following resection of HCC was defined based on the selection of relevant outcome parameters that represented the “optimal” patient outcome after surgery.^{7,11} TO parameters included negative margins, no reoperation, no postoperative complications (Clavien-Dindo grade III or more), no prolonged LOS (LOS \leq 75th percentile), no hospital readmission after discharge, and no postoperative mortality within 90 days after surgery. Tumor margin was categorized as microscopically negative (R0) or microscopically positive (R1); a positive resection margin (R1) was defined as either margin width less than 1 mm or involved margins. Patients with macroscopically positive margins (R2) were excluded. Reoperation was defined as return to the operating room within the index stay of the surgical procedure. Severity of complications was assessed according to the Clavien-Dindo classification system¹⁷; not experiencing complications categorized as grade III or higher was included in the definition of TO.¹⁸ Hospital readmission was defined as admission to index or non-index hospital within 30 days after discharge. Mortality was defined as death within 90 days of the index operation.¹⁹ Information on all 6 components of TO was extracted from each patient’s chart. When a patient experienced all six desired outcomes, the patient was categorized as having achieved a TO.

Statistical analysis

Categorical variables were presented as frequency (%), and continuous variables were presented as median and interquartile ranges (IQR). Patient, tumor and treatment characteristics were compared among patients who did and did not have a TO using the Pearson Chi-Square test for categorical and Kruskal-Wallis test for continuous variables, respectively. Multiple imputations were performed in case of missing data, which is an effective way to minimize bias and loss in precision rather than excluding such patients.^{20,21} Specifically, each missing value was replaced with probable estimates by creating 20 datasets through a chain

Table 1 Characteristics of patients undergoing curative-intent resection of HCC who achieved a TO vs. no TO

Characteristic	Total	No Textbook (n = 228)	Textbook (n = 377)	p-value
Sex				0.037
Male	463 (76.5%)	185 (81.1%)	278 (73.7%)	
Female	142 (23.5%)	43 (18.9%)	99 (26.3%)	
Age, years	67 (59–74)	68 (59–74)	66 (59–74)	0.28
ASA-PS				0.69
≤2	424 (70.1%)	162 (71.1%)	262 (69.5%)	
>2	181 (29.9%)	66 (28.9%)	115 (30.5%)	
Charlson Score				0.06
<3	192 (31.7%)	83 (36.4%)	109 (28.9%)	
≥3	413 (68.3%)	145 (63.6%)	268 (71.1%)	
BCLC stage				0.009
0	38 (6.3%)	6 (2.6%)	32 (8.5%)	
A	436 (72.1%)	162 (71.1%)	274 (72.7%)	
B/C	131 (21.6%)	60 (26.3%)	71 (18.8%)	
Cirrhosis				0.72
Yes	218 (36.2%)	80 (35.2%)	138 (36.7%)	
No	385 (63.8%)	147 (64.8%)	238 (63.3%)	
MIS				0.005
Yes	150 (24.8%)	42 (18.4%)	108 (28.6%)	
No	455 (75.2%)	186 (81.6%)	269 (71.4%)	
HBV infection				0.82
Yes	180 (29.7%)	65 (28.5%)	115 (30.5%)	
No	425 (70.3%)	162 (71.1%)	261 (69.2%)	
HCV infection				0.80
Yes	182 (30.1%)	70 (30.7%)	112 (29.7%)	
No	423 (69.9%)	158 (69.3%)	265 (70.3%)	
Grade				0.69
Well/Moderate	463 (78.2%)	174 (77.3%)	289 (78.7%)	
Poor/Undifferentiated	129 (21.8%)	51 (22.7%)	78 (21.3%)	
AFP, ng/mL	13.9 (4–250)	18.8 (4–512.6)	11.5 (3.00–144.0)	0.021
NLR	2.41 (1.62–3.42)	2.84 (2.06–3.65)	2.16 (1.56–3.29)	0.002
ALBI grade				0.038
1	341 (57.41)	115 (50.9%)	226 (61.4%)	
2 & 3	253 (42.59)	111 (49.1%)	142 (38.6%)	
Platelets, ×10 ³ /μL	188 (138–256)	187 (138–256)	193 (134–243)	0.56
Extent of Resection				0.004
Minor	365 (61%)	122 (53.7%)	243 (65.5%)	
Major	233 (39%)	105 (46.3%)	128 (34.5%)	
Albumin, g/dl	4 (3.6, 4.3)	3.9 (3.5–4.2)	4.1 (3.6–4.3)	0.016
LOS, days	8 (6–12)	13 (9–19)	7 (5–9)	<0.001
No. of tumor	1 (1–1)	1 (1–2)	1 (1–1)	0.31
Lympho-vascular involvement				0.014
No	343 (59.2%)	118 (52.9%)	225 (63.2%)	
Yes	236 (40.8%)	105 (47.1%)	131 (36.8%)	

(continued on next page)

Table 1 (continued)

Characteristic	Total	No Textbook (n = 228)	Textbook (n = 377)	p-value
Liver capsule involvement				0.011
No	303 (64.3%)	108 (57.4%)	195 (68.9%)	
Yes	168 (35.7%)	80 (42.6%)	88 (31.1%)	

ASA-PS= American Society of Anesthesiologists-Performance score; HBV = hepatitis B virus; HCV = hepatitis C virus; AFP = alpha-fetoprotein; NLR = neutrophil to lymphocyte ratio; BCLC= Barcelona Clinic Liver Cancer; ALBI = albumin-bilirubin; LOS = length of stay; MIS = minimally-invasive surgery.

equation method. Multivariable logistic regression was used to investigate possible associations among patient, tumor, treatment characteristics, and TO. A sensitivity analysis was performed to examine factors associated with TO after also adjusting for procedural volume. Further, to better understand the relationship between procedural volume and rates of TO, simple linear regression was utilized. A multivariable cox regression analysis was also performed to examine factors associated with overall survival (OS). A P-value <0.05 was considered statistically significant. All statistical analyses were performed with SAS 9.4 statistical software.

Results

A total of 605 patients who underwent curative-intent resection of HCC were included in the analytic cohort. The majority of patients were male (n = 463, 76.5%); median patient age was 67 years (IQR, 59–74). Most patients had BCLC-A HCC (n = 436, 72.1%), and the majority did not have liver cirrhosis (n = 385, 63.8%). Median tumor size was 5 cm (IQR, 3.2 cm–9.0 cm). Roughly one in four patients (n = 150, 24.8%) underwent

minimally invasive surgery and one third underwent major hepatectomy (n = 233, 39%). On final pathology, 78.2% (n = 463) of patients had well-to-moderately-differentiated tumors, whereas 129 patients (21.8%) had undifferentiated-to-poorly differentiated tumors. Lympho-vascular invasion and liver capsule involvement were present in 40.8% (n = 236) and 35.7% (n = 168) of tumor specimens, respectively. Resection margin status was microscopically negative (R0) in 542 (89.6%) patients and positive (R1) in 63 (10.4%) patients (Table 1).

Textbook Outcome following resection of HCC

The unadjusted incidence of TO ranged from 50.9% to 77.7% across the years of the study period. Fig. 1 depicts the frequency of each outcome indicator comprising the TO achieved among patients undergoing resection of HCC. While not experiencing a prolonged hospital stay (n = 451, 74.5%) had the greatest negative impact on the ability to obtain a TO, no reoperation (n = 593, 98.0%) was the outcome most commonly achieved among patients. In addition, 97.4% (n = 589) of patients did not die within 90 days following surgery, 94.4% (n = 571) did not experience a hospital readmission within 30 days, 89.6% (n = 542) did not die within 90 days following surgery, 88.6% (n = 536) did not experience a hospital readmission within 30 days, 74.5% (n = 451) did not experience a prolonged hospital stay, and 62.3% (n = 373) achieved a TO.

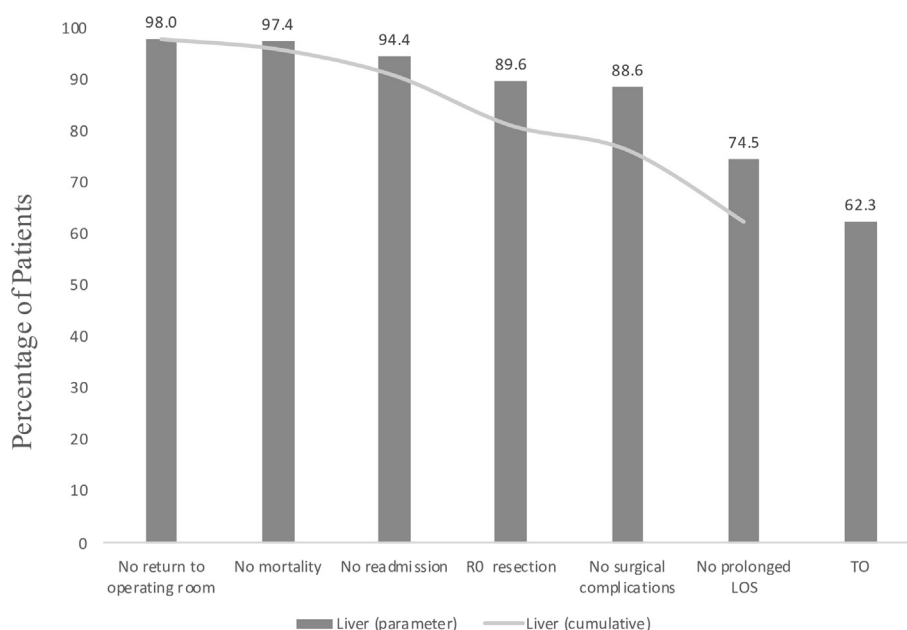


Figure 1 Textbook Outcome distribution stratified by the specific parameters among patients undergoing curative-intent resection of HCC

(n = 542) underwent an R0 resection and 88.6% (n = 536) of patients did not experience a surgical complication. Of note, while achievement of each individual quality metric was relatively high, an overall TO was achieved among only 62.3% (n = 377) of patients.

At the hospital level, the percentage of patients who achieved a TO ranged from 54.3% to 72.9%. Specifically, among patients treated at different institutions, the percentage of individuals who had R0 margins ranged from 86% to 100%, no prolonged LOS 66.6%–88.5%, no reoperation 94.3%–100%, no 90-day mortality 92%–100%, no 30-day readmission 87.3%–100%, and no surgical complications 78.2%–100%. While not experiencing a prolonged LOS had the greatest negative impact on achieving a TO in the majority of the participating centers, postoperative surgical complications was the major obstacle for TO among patients undergoing surgery in 2 of the institutions. Of note, there was no linear association between procedural volume and rates of TO at different centers (β coefficient = -0.08323 , p-value = 0.12).

Factors associated with achieving a Textbook Outcome

On multivariable analysis, after controlling for competing risk factors, individuals with BCLC-0 HCC were much more likely to achieve a TO compared with patients who had BCLC-B/C HCC (OR 4.17, 95%CI 1.62–10.7). In contrast, patients with BCLC-A HCC had comparable odds of achieving TO versus BCLC-B/C patients (OR 1.31, 95%CI 0.88–1.96). In addition, patients with an ALBI grade 1 had higher odds of achieving a TO compared with patients who had ALBI grade 2/3 (OR 1.49 95%CI 1.06–2.11) (Table 2). On sensitivity analysis, neither procedural volume (OR 0.97, 95%CI 0.95–1.01), nor ASA class (referent ≤ 2 : OR 1.12, 95%CI 0.68–1.75) and CCS (referent ≥ 3 : OR 0.58, 95%CI 0.35–1.41) were associated with TO. Rather, patients with HCV infection had lower odds of achieving a TO (OR 0.50, 95%CI 0.28–0.88), whereas ALBI grade 1 remained associated with higher odds of achieving a TO compared with ALBI grade 2 and 3 (OR 2.75 95%CI 1.66–4.75) (Supplemental Table 1).

Textbook Outcome and overall survival

Among patients who achieved a TO, 5-year OS was 69.6% versus 56.9% among individuals who did not achieve a TO (p < 0.001, Fig. 2). On multivariable analysis, after adjusting for competing factors, achieving a TO was associated with 40% decreased hazards of death (hazard ratio [HR] 0.60, 95% CI 0.42–0.85). In addition, BCLC stage 0 (referent BCLC B/C; HR 0.15, 95%CI 0.04–0.64), CCS <3 (HR 0.58, 95%CI 0.39–0.85), well/moderate tumor grade (HR 0.59, 95%CI 0.40–0.88) and ALBI grade 1 (HR 0.69, 95%CI 0.49–0.98) were independently associated with favorable outcomes, whereas the presence of lympho-vascular was associated with higher hazards of death (HR 1.63, 95%CI 1.12–2.37) (Table 3).

Discussion

TO is a multidimensional measure that more accurately represents the optimal clinical course of patients following a surgical episode.^{7,11} Rather than focusing on individual parameters, TO captures the entire surgical episode of care and provides a more patient-oriented estimate of quality of care. To this point, TO focuses on a more holistic patient-perceived outcome (i.e. were all the “good/expected” outcomes achieved), rather than

Table 2 Factors associated with achieving a TO

Variable	OR (95% CI)	P-value
Sex		
Female	Ref	
Male	0.89 (0.59–1.34)	0.56
Age		
≤ 65	Ref	
> 65	0.75 (0.52–1.06)	0.11
HBV infection		
No	Ref	
Yes	1.08 (0.74–1.59)	0.68
HCV infection		
No	Ref	
Yes	1.09 (0.75–1.58)	0.66
Charlson Score		
< 3	0.71 (0.487–1.03)	0.07
≥ 3	Ref	
Extent of surgery		
Major	Ref	
Minor	1.20 (0.81–1.78)	0.36
Type of resection		
Open	Ref	
MIS	0.85 (0.56–1.29)	0.45
BCLC stage		
0	4.17 (1.62–10.7)	0.005
A	1.31 (0.88–1.96)	0.09
B/C	Ref	
NLR	1.05 (0.95–1.16)	0.33
ASA-PS		
≤ 2	Ref	
> 2	0.92 (0.63–1.35)	0.66
AFP	1.01 (0.68–1.52)	0.95
ALBI grade		
1	1.49 (1.06–2.11)	0.02
2 & 3	Ref	

ASA-PS= American Society of Anesthesiologists-Performance score; HBV = hepatitis B virus; HCV = hepatitis C virus; AFP = alpha-fetoprotein; NLR = neutrophil to lymphocyte ratio; BCLC= Barcelona Clinic Liver Cancer; ALBI = albumin-bilirubin. Bold values represent statistical significance.

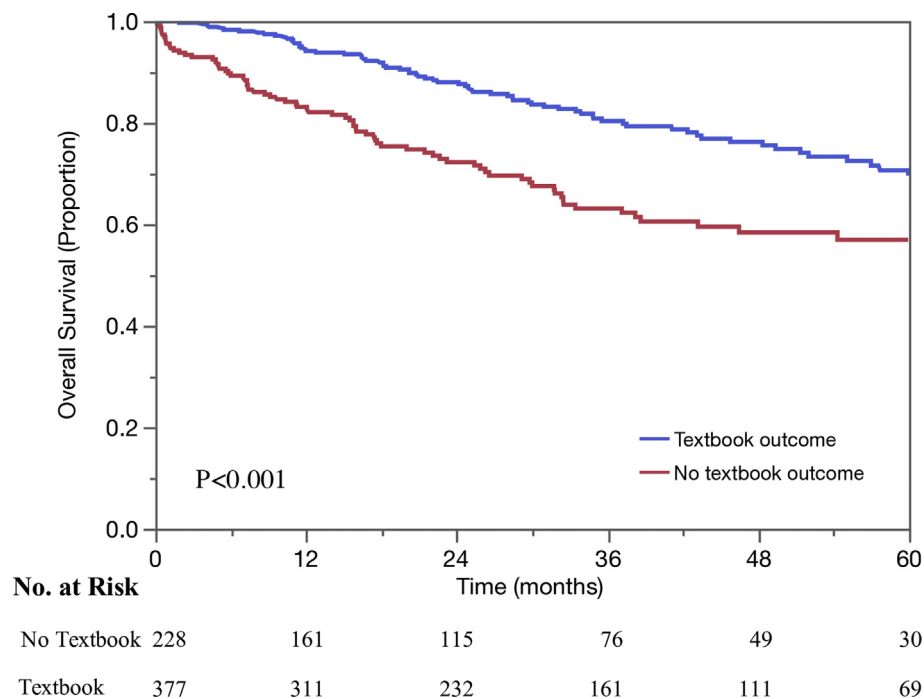


Figure 2 Kaplan–Meier curves depicting overall survival among patients undergoing resection of HCC stratified by whether TO was achieved

focusing on individual hospital-based metrics (i.e. the institution performed well in one quality area, yet poorly in another).^{7,11} The current study was important because we specifically defined TO among a population of patients undergoing resection of HCC and demonstrated that 6 in 10 patients ($n = 377$, 62.3%) achieved a TO. Specifically, across the study period examined, TO rates ranged from 50.9% to 77.7% at the patient level and 54.3%–72.9% at the hospital level. Of note, “no prolonged LOS” was the factor that was most attributable to patients not achieving a TO, followed by “no surgical complications” and “R0 resection”; in contrast, “no 90-day mortality” and “no 30-day readmission” were achieved in more than 90% of patients. Interestingly, achieving a TO was associated with an improved long-term outcome (5-year OS; TO vs non-TO: 69.6% vs 56.9%, $p < 0.001$), which persisted even after adjusting for competing factors (HR = 0.60, 95%CI 0.42–0.85; $p = 0.004$).

Quality of surgical care has primarily focused on outcomes such as morbidity, mortality, readmission and hospital LOS.^{22,23} However, analyzing indicators of care independently may prove problematic, since hospitals may perform well in one area yet worse in other areas. As such, reporting individual “siloe” quality parameters may not necessarily reflect the patient quality of care perspective – as patients experience composite outcomes. TO incorporates important aspects of the health care episode including oncologic (i.e. margin status), as well as quality (i.e. complications, readmission, length of stay, etc.) parameters.¹⁰ For example, margin status, even for early stage HCC, has important implications for patient outcomes including recurrence and survival.²⁴ In addition, the occurrence of postoperative

complications not only adversely affects short-term outcomes, but also has been associated with worse long-term prognosis.^{12,25,26} Recently, there has been increased interest in TO as a composite metric of quality with several investigators assessing the rates of TO among patients with cancer and vascular disease.^{7–11} To this point, in a previous study, our group noted that adjusted TO rates for Medicare beneficiaries undergoing liver surgery ranged from 16.6% to 78.7%.⁷

The current study showed that the overall incidence of TO was 62.3% on a per patient basis. Overall, the TO rate reported in the current study among patients with HCC undergoing liver resection was higher than previously reported following resection of other cancers such as esophageal (29.7%) and gastric cancer (32.1%).¹⁰ The reasons for these disparate results are undoubtedly multifactorial and may relate to differences in underlying patient cohorts (i.e. Medicare beneficiaries vs. all-comers), as well as variations inherent to different cancers, treatment regimens (i.e. use or no use of preoperative chemotherapy, etc.) and the definition of TO itself in the different studies. Of note, our results were in line with previous studies with regards to the reasons for not achieving a TO. Specifically, prolonged LOS was the main obstacle to achieve a TO followed by postoperative complications.^{7–10} On a hospital-level basis, the current study revealed that the percentage of patients who achieved a TO ranged from 54.3% to 72.9%. While prolonged LOS was the major obstacle for TO in the majority of centers, not experiencing postoperative surgical complications had the greatest negative impact on achieving a TO in 2 institutions. This may be related to the high inherent risk of complications among

Table 3 Factors associated with OS following resection of HCC

Variable	HR (95% CI)	P-value
Sex		
Male	1.07 (0.71–1.62)	0.74
Female	Ref	
Age		
≤65	Ref	
>65	1.32 (0.92–1.89)	0.13
Charlson Score		
<3	0.58 (0.39–0.85)	0.006
≥3	Ref	
BCLC stage		
0	0.15 (0.04–0.64)	0.01
A	0.70 (0.47–1.03)	0.07
B/C	Ref	
AFP	1.25 (0.83–1.88)	0.27
Textbook Outcome		
No	Ref	
Yes	0.60 (0.42–0.85)	0.004
ALBI grade		
1	0.69 (0.49–0.98)	0.037
2 & 3	Ref	
Grade		
Well/Moderate	0.59 (0.40–0.88)	0.008
Poor/Undifferentiated	Ref	
Lympho-vascular Invasion		
Yes	1.63 (1.12–2.37)	0.01
No	Ref	
Liver Capsule Involvement		
Yes	1.05 (0.72–1.53)	0.81
No	Ref	

AFP = alpha-fetoprotein; BCLC= Barcelona Clinic Liver Cancer; ALBI = albumin-bilirubin.

Bold values represent statistical significance.

patients with HCC, many of whom have underlying liver disease and other comorbidities.^{27,28} Overall, approximately 6 in 10 patients who underwent resection of HCC achieved a complete TO even at the high-volume tertiary centers, which constituted the multi-institutional collaboration. While TO as a metric of quality may not be ideal and will require future refinements, several leaders in quality and hepato-pancreatic-biliary surgery have advocated for TO as a means to demonstrate variation among hospitals and recognize best practices.²⁹

Several factors were associated with the chance of achieving TO after resection of HCC. Perhaps not surprisingly, patients with BCLC stage 0 HCC were much more likely to achieve a TO compared with patients who had more advanced tumors (i.e. BCLC B/C). However, BCLC-A patients had comparable odds of a TO versus patients undergoing resection for multinodular

HCC (BCLC-B) or HCC with vascular invasion (BCLC-C) (Table 2). Patients with lower ALBI grade also more often achieved a TO following resection for HCC, consistent with data showing that ALBI was as a surrogate of liver function reserve.^{30,31} While BCLC stage and ALBI have previously been well-established as predictive of long-term survival,^{30,32,33} the independent impact of TO relative to prognosis has not been well-studied. As such, the current study revealed that patients who achieved a TO had a better 5-year overall survival compared with individuals who did not (69.6% vs. 56.9%, $p < 0.001$), which persisted on multivariable analysis after adjusting for competing factors (HR = 0.60, 95% CI 0.42–0.85). Van der Kaaij and colleagues had similarly reported better long-term survival among patients achieving a TO following surgery for esophageal cancer.³² Collectively, the data suggest that TO may be associated with both optimal short- and long-term outcome among patients undergoing complex surgical procedures.

Several limitations should be considered when interpreting the results of the current study. As with all retrospective studies, selection bias was possible. The ability to achieve a TO is undoubtedly derivative from optimal patient selection. As such, the incidence of TO may vary based on how well the surgical cohort is selected. In addition, data on patient-reported outcomes, quality of life, and health care costs were not available in the dataset to correlate with TO. Furthermore, although the multi-institutional nature of the cohort was a strength, there was likely some heterogeneity in patient selection, surgical technique, as well as treatment strategy according to the practices at the individual centers.

In conclusion, while postoperative mortality occurred in less than 3% of patients in specialized centers, only 6 in 10 patients achieved a TO following resection for HCC. Among the TO indicators, prolonged LOS was the factor mostly associated with an inability to achieve a TO, while “postoperative surgical complications” was the major obstacle for TO in 2 of the participating centers. While marked variation in the rate of TO was noted at both the patient and hospital level, when achieved, TO was associated with better long-term outcomes following resection of HCC. While TO should not be used to lead centers to avoid certain patients and operate only on the very best candidates, reporting TO among tertiary hepatobiliary institutions does serve to highlight that physicians and hospitals still have a long way to go to optimize the “real world” outcomes of our patients following resection of HCC. Data from the current study demonstrated that TO is a simple composite measure of both short- and long-term outcomes among patients undergoing resection for HCC. As such, TO could prove an important tool to assess patient-level hospital performance and help more realistically inform patients about more holistic expected outcomes following surgery for HCC.

Acknowledgements

None.

Funding

None.

Conflict of interest

None declared.

References

- Medicine Io. (2006) *Performance Measurement: Accelerating Improvement*. Washington, DC: The National Academies Press.
- Dimick JB, Staiger DO, Baser O, Birkmeyer JD. (Jul-Aug 2009) Composite measures for predicting surgical mortality in the hospital. *Health Aff* 28:1189–1198, 2009.
- Dimick JB, Birkmeyer NJ, Finks JF, Share DA, English WJ, Carlin AM *et al.* (Jan 2014) Composite measures for profiling hospitals on bariatric surgery performance. *JAMA Surg* 149:10–16.
- Dimick JB, Staiger DO, Osborne NH, Nicholas LH, Birkmeyer JD. (Oct 2012) Composite measures for rating hospital quality with major surgery. *Health Serv Res* 47:1861–1879.
- Staiger DO, Dimick JB, Baser O, Fan Z, Birkmeyer JD. (Feb 2009) Empirically derived composite measures of surgical performance. *Med Care* 47:226–233.
- Shwartz M, Restuccia JD, Rosen AK. (Dec 2015) Composite measures of health care provider performance: a description of approaches. *Milbank Q* 93:788–825.
- Merath K, Chen Q, Bagante F, Beal E, Akgul O, Dillhoff M *et al.* (Nov 29 2018) Textbook outcomes among Medicare patients undergoing hepatopancreatic surgery. *Ann Surg* [Epub ahead of print].
- Kolfschoten NE, Kievit J, Gooiker GA, van Leersum NJ, Snijders HS, Eddes EH *et al.* (Feb 2013) Focusing on desired outcomes of care after colon cancer resections; hospital variations in 'textbook outcome'. *Eur J Surg Oncol* 39:156–163.
- Karthauss EG, Lijftogt N, Busweiler LAD, Elsmann BHP, Wouters M, Vahl AC *et al.* (Nov 2017) Textbook outcome: a composite measure for quality of elective aneurysm surgery. *Ann Surg* 266:898–904.
- Busweiler LA, Schouwenburg MG, van Berge Henegouwen MI, Kolfschoten NE, de Jong PC, Rozema T *et al.* (May 2017) Textbook outcome as a composite measure in oesophagogastric cancer surgery. *Br J Surg* 104:742–750.
- Merath K, Chen Q, Bagante F, Alexandrescu S, Marques HP, Aldrighetti L *et al.* (Apr 2019) A multi-institutional international analysis of textbook outcomes among patients undergoing curative-intent resection of intrahepatic cholangiocarcinoma. *JAMA Surg* 190:571.
- Margonis GA, Sasaki K, Andreatos N, Nishioka Y, Sugawara T, Amini N *et al.* (2017) Prognostic impact of complications after resection of early stage hepatocellular carcinoma. *J Surg Oncol* 115:791–804.
- Margonis GA, Sasaki K, Andreatos N, Nishioka Y, Sugawara T, Amini N *et al.* (Dec 2019) Defining the chance of cure after resection for hepatocellular carcinoma within and beyond the Barcelona Clinic Liver Cancer guidelines: a multi-institutional analysis of 1,010 patients. *Surgery* 166(6):967–974.
- European Association for the Study of the Liver. (Jul 2018) Electronic address eee, European association for the study of the L. EASL clinical practice guidelines: management of hepatocellular carcinoma. *J Hepatol* 69:182–236.
- Strasberg SM. (2005) Nomenclature of hepatic anatomy and resections: a review of the Brisbane 2000 system. *J Hepatobiliary Pancreat Surg* 12: 351–355.
- Johnson PJ, Berhane S, Kagebayashi C, Satomura S, Teng M, Reeves HL *et al.* (Feb 20 2015) Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. *J Clin Oncol: Off J Am Soc Clin Oncol* 33:550–558.
- Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD *et al.* (Aug 2009) The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 250:187–196.
- van Roessel S, Mackay TM, van Dieren S, van der Schelling GP, Nieuwenhuijs VB, Bosscha K *et al.* (Jul 3 2019) Textbook outcome: nationwide analysis of a novel quality measure in pancreatic surgery. *Ann Surg* [Epub ahead of print].
- Mayo SC, Shore AD, Nathan H, Edil BH, Hirose K, Anders RA *et al.* (Jul 2011) Refining the definition of perioperative mortality following hepatectomy using death within 90 days as the standard criterion. *HPB* 13: 473–482.
- Perkins NJ, Cole SR, Harel O, Tchetgen Tchetgen EJ, Sun B, Mitchell EM *et al.* (Mar 1 2018) Principled approaches to missing data in epidemiologic studies. *Am J Epidemiol* 187:568–575.
- Donders AR, van der Heijden GJ, Stijnen T, Moons KG. (Oct 2006) Review: a gentle introduction to imputation of missing values. *J Clin Epidemiol* 59:1087–1091.
- Dimick JB, Welch HG, Birkmeyer JD. (Aug 18 2004) Surgical mortality as an indicator of hospital quality: the problem with small sample size. *JAMA* 292:847–851.
- Lawson EH, Zingmond DS, Stey AM, Hall BL, Ko CY. (Oct 2014) Measuring risk-adjusted value using Medicare and ACS-NSQIP: is high-quality, low-cost surgical care achievable everywhere? *Ann Surg* 260: 668–677. discussion 677–669.
- Tsilimigras DI, Sahara K, Moris D, Hyer JM, Paredes AZ, Bagante F *et al.* (Jun 26 2019) Effect of surgical margin width on patterns of recurrence among patients undergoing R0 hepatectomy for T1 hepatocellular carcinoma: an international multi-institutional analysis. *J Gastrointest Surg* [Epub ahead of print].
- Spolverato G, Yakoob MY, Kim Y, Alexandrescu S, Marques HP, Lamelas J *et al.* (Aug 15 2015) Impact of complications on long-term survival after resection of intrahepatic cholangiocarcinoma. *Cancer* 121:2730–2739.
- Mavros MN, de Jong M, Dogeas E, Hyder O, Pawlik TM. (Apr 2013) Impact of complications on long-term survival after resection of colorectal liver metastases. *Br J Surg* 100:711–718.
- Sasaki K, Shindoh J, Margonis GA, Nishioka Y, Andreatos N, Sekine A *et al.* (Mar 15 2017) Effect of background liver cirrhosis on outcomes of hepatectomy for hepatocellular carcinoma. *JAMA Surg* 152:e165059.
- Pawlik TM, Poon RT, Abdalla EK, Ikai I, Nagorney DM, Belghiti J *et al.* (Apr 2005) Hepatectomy for hepatocellular carcinoma with major portal or hepatic vein invasion: results of a multicenter study. *Surgery* 137: 403–410.
- Pitt HA. (Aug 2019) Benchmark, textbook or optimal pancreatic surgery? *Ann Surg* 270:219–220.
- Tsilimigras DI, Hyer JM, Moris D, Sahara K, Bagante F, Guglielmi A *et al.* (Apr 25 2019) Prognostic utility of albumin-bilirubin grade for short- and long-term outcomes following hepatic resection for intrahepatic cholangiocarcinoma: a multi-institutional analysis of 706 patients. *J Surg Oncol*.
- Andreatos N, Amini N, Gani F, Margonis GA, Sasaki K, Thompson VM *et al.* (Feb 2017) Albumin-bilirubin score: predicting short-term

- outcomes including bile leak and post-hepatectomy liver failure following hepatic resection. *J Gastrointest Surg* 21:238–248.
- 32.** van der Kaaij RT, de Rooij MV, van Coevorden F, Voncken FEM, Snaebjornsson P, Boot H *et al.* (Apr 2018) Using textbook outcome as a measure of quality of care in oesophagogastric cancer surgery. *Br J Surg* 105:561–569.
- 33.** Tsilimigras DI, Bagante F, Sahara K, Moris D, Hyer JM, Wu L *et al.* (Oct 2019) Prognosis after resection of Barcelona clinic liver cancer (BCLC)

stage 0, A, and B hepatocellular carcinoma: a comprehensive assessment of the current BCLC classification. *Ann Surg Oncol* 26(11): 3693–3700.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.hpb.2019.12.005>.